Schering-Plough

Schering Canada Inc.
3535 Trans-Canada
Pointe Claire, Quebec
Canada H9R 1B4

MATERIAL SAFETY DATA SHEET

Schering-Plough urges each user or recipient of this MSDS to read the entire data sheet to become aware of the hazards associated with this material.

SECTION 1. IDENTIFICATION OF SUBSTANCE AND CONTACT INFORMATION

MSDS NAME: **Florfenicol Powders**

SYNONYM(S): Aquaflor Medicated Premix for Salmon
Florocol
Aquacol VET Medicated Premix for Salmon

MSDS NUMBER: SP000956

EMERGENCY NUMBER(S): Schering-Plough Security Control Center (908) 820-6921 (24 Hours)

Transportation Emergencies -
CANUTEC: (613) 996-6666 (Canada)

INFORMATION: Animal Health Technical Services:
(888) 306-0069 (Canada)

SCHERING-PLOUGH MSDS HELPLINE: (800) 770-8878 (US and Canada)
(908) 629-3657 (Worldwide)
Monday to Friday, 9am to 5pm (US Eastern Time)

SECTION 2. COMPOSITION AND INFORMATION ON INGREDIENTS

PRODUCT USE: Aquaculture product

CHEMICAL FORMULA: Mixture.

The formulations for these products are proprietary information. These formulations have the same hazardous profile; however, the presence of hazardous ingredients may vary by formulation. Only hazardous ingredients in concentrations of 1% or greater and/or carcinogenic ingredients in concentrations of 0.1% or greater are listed in the Chemical Composition table. Active ingredients in any concentration are listed. For additional information about carcinogenic ingredients see Section 3.

HAZARDOUS COMPONENTS

CHEMICAL NAME	CAS NUMBER	PERCENT
Florfenicol	76639-94-6	50-60
Lactose	63-42-3	40-50
Povidone	9003-39-8	1-10

ADDITIONAL INFORMATION: This MSDS is written to provide health and safety information for individuals who will be handling the final product formulation during research, manufacturing, and distribution. For health and safety information for individual ingredients used during manufacturing, refer to the appropriate MSDS for each ingredient. Refer to the package insert or product label for handling guidance for the consumer.

SECTION 3: HAZARDS IDENTIFICATION

EMERGENCY OVERVIEW

White
Powder
Odor unknown

May cause allergic reactions in susceptible individuals.

May cause effects to:
- gastrointestinal tract
- male reproductive system

May cause impaired fertility.
May cause developmental effects.

Toxic to fish and aquatic organisms.
May cause long-term adverse effects in the aquatic environment.

POTENTIAL HEALTH EFFECTS:

The following summary is based upon available information about the individual ingredients of the mixture, or of the expected properties of the mixture.

This product is not for use in humans. Clinical effects in humans have not been determined.

Florfenicol, the active ingredient in this product, is a broad spectrum antibiotioc used in veterinary products. Florfenicol may cause allergic reactions in susceptible individuals. Based on animal studies, florfenicol may cause slight eye irritation, constipation, changes in blood cell counts, changes in stool, or liver effects. It may also cause developmental effects or effects to male reproductive organs.

Lactose is not expected to produce significant toxicity with workplace exposure. Lactose may cause irritation to the eyes, skin, and mucous membranes from mechanical action. Lactose may cause abdominal pain, bloating and diarrhea if ingested in large amounts or in lactose-intolerant individuals. Lactose may cause allergic reactions in sensitive individuals.

Povidone is not-irritating, not-sensitizing and practically not-toxic. Because povidone is not absorbed from the gastrointestinal tract, at high concentrations povidone can cause increased bowel activity, flatulence (gas), and severe constipation. These effects are not expected with occupational handling of the material.

LISTED CARCINOGENS

CHEMICAL NAME	CAS NUMBER	OSHA	IARC	NTP	ACGIH
Povidone	9003-39-8		Not classifiable.		

SECTION 4: FIRST AID MEASURES

INHALATION: Remove to fresh air. If any trouble breathing, get immediate medical attention. Administer artificial respiration if breathing has ceased. If irritation or symptoms occur or persist, consult a physician.

SKIN CONTACT: In case of skin contact, while wearing protective gloves, carefully remove any contaminated clothing, including shoes, and wash skin thoroughly with soap and water. If irritation or symptoms occur or persist, consult a physician.

EYE CONTACT: In case of eye contact, immediately rinse eyes thoroughly with plenty of water. If wearing contact lenses, remove only after initial rinse, and continue rinsing eyes for at least 15 minutes. If irritation occurs or persists, consult a physician.

INGESTION: Rinse mouth and drink a glass of water. Do not induce vomiting. If symptoms persist, consult a physician.

NOTE TO PHYSICIAN: This product contains florfenicol, a broad spectrum antibiotic which may cause allergic reactions in susceptible individuals.

SECTION 5: FIRE FIGHTING MEASURES

FLAMMABILITY DATA:

FLASH POINT: Not determined (liquids) or not applicable (solids).

OTHER EXPLOSION HAZARDS:
Under normal conditions of use, this material does not present a significant fire or explosion hazard. However, like most organic compounds, this material may present a dust deflagration hazard if sufficient quantities are suspended in air. This hazard may exist where sufficient quantities of finely divided material are (or may become) suspended in air during typical process operations. An assessment of each operation should be conducted and suitable deflagration prevention and protection techniques employed.

The sensitivity of this material to ignition by electrostatic discharges has not been determined. In the absence of testing data, all conductive plant items and operations personnel handling this material should be suitably grounded.

SPECIAL FIRE FIGHTING PROCEDURES:
Wear full protective clothing and self-contained breathing apparatus (SCBA).

SUITABLE EXTINGUISHING MEDIA:
Carbon dioxide (CO_2), extinguishing powder or water spray.

See Section 9 for Physical and Chemical Properties.

SECTION 6: ACCIDENTAL RELEASE MEASURES

PERSONAL PRECAUTIONS:
Keep personnel away from the clean-up area. Wear appropriate personal protective equipment as specified in Section 8. Avoid generation of dust during clean-up.

SPILL RESPONSE / CLEANUP:
All spills should be handled according to site requirements and based on precautions cited in the MSDS. In the case of liquids, use proper absorbent materials. In manufacturing and large-scale operations, HEPA vacuuming prior to wet mopping or cleaning is required.

ENVIRONMENTAL PRECAUTIONS:
This product is toxic to fish and/or aquatic organisms. Do not allow product to reach ground water, water course, sewage or drainage systems.

See Sections 9 and 10 for additional physical, chemical, and hazard information.

SECTION 7: HANDLING AND STORAGE

HANDLING:
Avoid dust generation. Keep containers adequately sealed during material transfer, transport, or when not in use.

Appropriate handling of this material is dependent on many factors, including physical form, duration and frequency of process or task, and effectiveness of engineering controls. Site-specific risk assessments should be conducted to determine the feasibility and the appropriateness of all exposure control measures. See Section 8 (Exposure Controls) for additional guidance.

STORAGE:
Store in a cool, dry, well ventilated area.

See Section 8 for exposure controls and additional safe handling information.

SECTION 8: EXPOSURE CONTROLS AND PERSONAL PROTECTION

The following guidance applies to the handling of the active ingredient in this formulation.

S-P OCCUPATIONAL EXPOSURE GUIDELINE (OEG): Schering-Plough Corporation has established an Occupational Exposure Guideline (OEG) of 180 mcg/m^3 (8-hr TWA) for Florfenicol. Consult your site safety professional for additional guidance.

EXPOSURE CONTROLS:
The health hazard risks of handling this material are dependent on many factors, including physical form, duration and frequency of process or task, and effectiveness of engineering controls. Site-specific risk assessments should be conducted to determine the feasibility and the appropriateness of all exposure control measures. Exposure controls for normal operating or routine procedures follow a tiered strategy. Engineering controls are the preferred means of long-term or permanent exposure control. If engineering controls are not feasible, substitution of approved materials or appropriate use of personal protective equipment (PPE) may be considered as alternative control measures. However, PPE should not be used as a method of permanent or long-term exposure control. Exposure controls for non-routine operations must be evaluated and addressed as part of the site-specific risk assessment.

RECOMMENDED PERSONAL PROTECTIVE EQUIPMENT (PPE):

Respiratory Protection:	Respirators are not normally required; however, appropriate respiratory protection may be required in situations where exposure (e.g. spills, process upsets, or non-routine maintenance) may exceed any available recommended exposure limit. Consult your site safety staff for guidance.
Skin Protection:	Gloves that provide an appropriate barrier to the skin are recommended if there is potential for contact with this material. Consult your site safety staff for guidance.
Eye Protection:	Safety glasses with side shields. Use of goggles or full face protection may be required if there is potential for contact with this material. Consult your site safety staff for guidance.
Body Protection:	In small scale or laboratory operations, lab coats or other equivalent protective clothing is required. In large-scale or manufacturing operations, lab coats or other equivalent protective clothing is required.

EXPOSURE LIMIT VALUES

See Schering-Plough occupational exposure guideline (OEG) listed above.

SECTION 9: PHYSICAL AND CHEMICAL PROPERTIES

FORM:	Powder
COLOR:	White
ODOR:	Odor unknown
SOLUBILITY:	
Water:	Florfenicol: 1.32 mg/mL at pH7
Acetone:	Florfenicol: Very soluble

See Section 5 for flammability/explosivity information.

SECTION 10: STABILITY AND REACTIVITY

STABILITY/ REACTIVITY:
Stable under normal conditions.

INCOMPATIBLE MATERIALS / CONDITIONS TO AVOID:
Open flames and high temperatures.

HAZARDOUS DECOMPOSITION PRODUCTS / REACTIONS:
Carbon oxides (COx).

SECTION 11: TOXICOLOGICAL INFORMATION

The toxicological properties of this mixture have not been fully characterized in humans or animals. The information presented below pertains to the following individual ingredients, and not to the mixture.

ACUTE TOXICITY DATA

INHALATION:
Rats exposed to florfenicol for 4 hours showed dry rales, anogenital staining, secretory discharge, soft stool, and decreased body weights. These effects were seen immediately or up to one-week post exposure. Some effects did not resolve by study termination. The inhalation LC50 (4 hr) was >0.28 mg/L in rats.

SKIN:
Florfenicol was not irritating to rabbit skin (PII = 0) Povidone did not produce primary dermal irritation in a human repeated insult patch test.

EYE:
Florfenicol was slightly irritating to the eyes of rabbits. Povidone did not produce ocular irritation in rabbits.

ORAL:
Florfenicol: Oral LD50: >2000 mg/kg (rat, mouse).
Dogs (one animal/sex) were administered successive oral doses of florfenicol that ranged from 160 to 1280 mg/kg. No clinical effects occurred at doses as high as 640 mg/kg. At 640 mg/kg, the only female died from inhalation of vomitus. Vomiting or soft stool occurred at 640 to 1280 mg/kg.

Lactose: Oral LD50: > 10g/kg (rat)
Povidone: (LD50 values vary based on molecular weight):
Rat (Oral) LD50: >100 g/kg (PVP K-30, molecular weight 40,000)
Rat (Oral) LD50: 8.25 g/kg (unspecified molecular weight)

SENSITIZATION:
Florfenicol was not a skin sensitizer in guinea pigs.
Povidone did not produce sensitization in a human repeated insult patch test.

REPEAT DOSE TOXICITY DATA

SUBCHRONIC / CHRONIC TOXICITY:
Florfenicol was administered orally to dogs, rats, and mice at dosages as high as 100 to 400 mg/kg/day for up to 13 weeks. Effects including decreased body weight, changes in liver weight or liver enzyme levels, changes in testicular weight, testicular atrophy, decreased white blood cell counts, and decreased hemoglobin levels were observed at high dosages. Cellular changes in the liver or lymph nodes of rats and mice, and histopathologic changes in the brain and spinal cord of dogs were also noted at these high dosages. Although some effects were reversible after a 4-week withdrawal from treatment, testicular effects in rats persisted. Intramuscular injections of 45 mg/kg of florfenicol in swine produced diarrhea, injection site lesions, decreased body weight, decreased food and water consumption, changes in serum electrolytes and proteins, decreased red blood cell and white blood cell counts, decreased spleen weight, and decreased kidney weight.

In 52-week oral toxicity studies in dogs and rats, high dosages of florfenicol (12 and 48 mg/kg/day, respectively) increased liver weight and produced cellular changes in the gall bladder of dogs. In rats, florfenicol at the high dosage reduced body weight gain, reduced testicular weight, induced changes in hematologic and clinical chemistry parameters, and increased the incidence of testicular tubular atrophy. In two-year chronic studies in mice and rats, florfenicol caused similar effects as those observed in other long-term studies including reduced body weight gain, reduced red blood cell count, reduced hemoglobin levels, and testicular effects such as small testes, tubular atrophy and aspermatogenesis in both the high dosage rats (48 mg/kg/day) and mice (200 mg/kg/day).

Povidone fed to rats and dogs at 10% in the diet for 90 or 28 days, respectively, had no effect in rats; in dogs it increased spleen weight and accumulated in the mesenteric lymph nodes.

REPRODUCTIVE / DEVELOPMENTAL TOXICITY:
In a two-generation reproductive study, oral administration as high as 12 mg/kg/day of florfenicol reduced epididymal weights, decreased pup survival, and reduced lactation index in rats [NOAEL: 3 mg/kg/day].

There was no evidence of teratogenicity in rats administered florfenicol at dosages of 4, 12 or 40 mg/kg/day. Slight maternal toxicity, evidenced by decreased food and water consumption, was observed above 4 mg/kg/day. At 40 mg/kg/day, an increased incidence of delayed ossification and decreased fetal weight occurred. The NOAEL for maternal and fetal toxicity in rats was determined to be 4 mg florfenicol/kg/day.

Two teratogenicity studies were performed in mice. In the first study, the mice were administered florfenicol at dosages of 40, 120, or 400 mg/kg by gavage on days 6-15 of gestation. Florfenicol produced embryolethality at the 400 mg/kg/day dose level, which was evidenced by the high incidence of intrauterine deaths. Significant decreases in mean fetal body weight, soft tissue defects, and retarded skeletal ossification were also observed at 400 mg/kg/day. Skeletal ossification was less pronounced, in a dose-related fashion, at the lower doses tested (40 and 120 mg/kg/day). A developmental NOAEL could not be determined for these data [NOAEL for maternal: 120 mg/kg]. In the second teratogenicity study, florfenicol was retested at lower administered dosages of 1, 3, or 60 mg/kg/day. Maternal effects were limited to a slight increase in water consumption at the 60 mg/kg/day dose. There was no evidence of any adverse effects on the embryo/fetus at doses as high as 60 mg/kg/day in this study. However, based upon the retarded skeletal ossification effects observed in the first study at 40 mg/kg/day the NOAEL for the two studies combined was determined to be between 3 and 40 mg/kg/day.

Pregnancy rate and fetal parameters were unaffected in rabbits given povidone at 1250 mg/kg/day (IV), and in rats fed 10% povidone in the diet.

MUTAGENICITY / GENOTOXICITY:
Florfenicol was negative in a bacterial mutagenicity study (Ames), a mammalian mutagenicity study (mouse lymphoma), a bone marrow micronucleus assay, an in vitro chromosomal aberration assay in CHO cells, a cytogenetics assay in bone marrow, and an unscheduled DNA synthesis assay in rat hepatocytes.

Povidone was negative in a bacterial mutagenicity study (Ames), mammalian mutagenicity study (mouse lymphoma), mouse dominant lethal assay, chromosomal aberration assay, and BALB/C3T3 transformation assay.

CARCINOGENICITY:
This material has not been evaluated for carcinogenicity.

Florfenicol was not carcinogenic in a 2-year study in rats administered dosages up to 48 mg/kg/day for 5 days a week or in mice at dosages up to 200 mg/kg/day for 5 days per week.

In combined chronic toxicity and oncogenicity studies conducted in dogs and rats, there was no evidence of carcinogenicity when povidone was given at 10% concentration in the diet.

SECTION 12. ECOLOGICAL INFORMATION

This information presented below pertains to the following ingredient(s) and does not apply to the final product or its formulation(s).

ECOTOXICITY DATA

INGREDIENT ECOTOXICITY

Florfenicol: 96-hr LC50 (bluegill): >830 mg/L
Florfenicol: 96-hr LC50 (trout): >780 mg/L
Florfenicol: 48-hr EC50 (daphnid): >330 mg/L
Florfenicol: Algae maximum cell density: MIC = 1.5 mg/L
Florfenicol: Algae maximum growth rate: MIC >2.9 mg/L

ENVIRONMENTAL DATA

OTHER INGREDIENT ENVIRONMENTAL DATA:

Florfenicol is not readily biodegradable but there is evidence of inherent biodegradability.

SECTION 13. DISPOSAL CONSIDERATIONS

MATERIAL WASTE:
Disposal must be in accordance with applicable federal, state/provincial, and/or local regulations. Incineration is the preferred method of disposal, when appropriate. Operations that involve the crushing or shredding of waste materials or returned goods must be handled to meet the ECG or OEG.

PACKAGING AND CONTAINERS:
Disposal must be in accordance with applicable federal, state/provincial, and/or local regulations.

SPECIAL ENVIRONMENTAL HANDLING PROCEDURES:
This product contains materials that are harmful to the environment. Do not allow product to reach ground water, water courses, sewage or drainage system.

SECTION 14. TRANSPORT INFORMATION

This material is not subject to the transportation regulations of DOT, ICAO, IMO, and the ADR.

SECTION 15. REGULATORY INFORMATION

TSCA LISTING

CHEMICAL NAME	TSCA
Lactose	Listed
Povidone	Listed

WHMIS CLASSIFICATIONS:

This product has been classified in accordance with the hazard criteria on the Controlled Products Regulations and the MSDS contains all the information required by the Controlled Products Regulations.

The final packaged product is not subject to WHMIS classification. The following classification applies to the bulk formulation handled in the workplace.

Controlled Product Class: D2A: Very Toxic

SECTION 16: OTHER INFORMATION

Although reasonable care has been taken in the preparation of this document, we extend no warranties and make no representations as to the accuracy or completeness of the information contained therein, and assume no responsibility regarding the suitability of this information for the user's intended purposes or for the consequence of its use. Each individual should make a determination as to the suitability of the information for their particular purpose(s).

DEPARTMENT ISSUING MSDS:

Global Safety and Environmental Affairs
Occupational and Environmental Toxicology
Schering-Plough Corporation
1095 Morris Avenue
Union, NJ 07083 USA

SCHERING-PLOUGH MSDS HELPLINE:

(800) 770-8878 (US and Canada)
(908) 629-3657 (Worldwide)
Monday to Friday, 9am to 5pm (US Eastern Time)

MSDS CREATION DATE: 12-Nov-1992
SUPERSEDES DATE: 05-Dec-2003